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10/536,802	09/22/2005	Tsukasa Seya	GRT/1035-591	4531

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EXAMINER	
HAMUD, FOZIA M	
ART UNIT	PAPER NUMBER
1647	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,802	SEYA ET AL.	
	Examiner	Art Unit	
	FOZIA M. HAMUD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6,9,27 and 33-37* is/are pending in the application.

4a) Of the above claim(s) *1,2,4,6,9,27 and 37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3 and 33-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *27 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Applicant's Amendment:

1a. Applicants' amendment filed on 28 March 2008 has been entered.

Status of Claims

1b. Claims 5, 7-8, 10-26 and 28-32 have been cancelled. New claim 37 has been added. Thus, claims 1-4, 6, 9, 27 and 33-37 are pending.

1c. Newly submitted claim 37 and amended claims 1, 2, 4, 6, 9 and 27 are directed to inventions that are independent or distinct from the invention originally claimed for the following reasons:

I. The examined claims were drawn to a cell comprising a vector comprising a gene that encodes the protein of SEQ ID NO: 2, or that encodes a protein that comprises amino acids 394-532 of SEQ ID NO:2, a method of screening using said cell, said gene and the encoded polypeptides.

II. Amended claims 1-2, 27, are drawn to a method of inducing interferon beta production by using a vector comprising a gene that encodes a protein of SEQ ID NO: 2, or that encodes a protein that comprises amino acids 394-532 of SEQ ID NO:2.

III. Amended claims 4, 6 and 9 are drawn to a method of treating cancer administering a cell including a vector comprising a gene that encodes a protein of SEQ ID NO: 2, or that encodes a protein that comprises amino acids 394-532 of SEQ ID NO:2.

IV. New claim 37 is drawn to a method of inhibiting interferon beta by using a vector comprising a gene that encodes a protein that comprises amino acids 394-532 of SEQ ID NO:2, wherein proline at position 434 is replaced with a histidine.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 1, 2, 4, 6, 9, 27 and 37 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Thus claims 3 and 33-36 are drawn to the elected invention and are under consideration.

Specification:

2. The amendment to the specification providing sequence identifiers is acknowledged. No new matter is added.

Response to Applicant's Argument:

3. The following rejections are withdrawn in light of Applicants' amendments:

I. All of the rejections against cancelled claims 5, 7-8, and 25, 27, 29, 31-32 are moot.

II. All of the rejections against claims 1, 2, 4, 6, 9 and 27 are moot, since these claims now encompass an invention different from the one that was examined.

III The rejection of claims 33 and 34 made under 35 U.S.C. 101 for encompassing a naturally occurring product is withdrawn, because the amended claims now encompass isolated products.

III. The rejection of claim 3 made under 35 U.S.C § 102(b) as being anticipated Lal et al, (WO200078954-A2, issued on 28 December 2000), or Accession Number: O75532, published on 01 November 1998 or Matsuda et al, (WO2002053737-A1, issued on 11 July 2002), is withdrawn. None of the references teach that the protein of SEQ ID NO:2 or a protein comprising amino acids 395-532 binds TLR3, therefore, the claimed method is not anticipated.

IV. The rejection of claims 33-36 made under 35 U.S.C § 102(b) as being anticipated Matsuda et al, (WO2002053737-A1, issued on 11 July 2002), because Matsuda et al does not disclose an isolated protein comprising amino acids 394-532 of SEQ ID NO:2, wherein proline at position 434 is replaced with a histidine, wherein said protein binds toll like receptor 3 (TLR3), but does not induce interferon beta (IFN-β) production.

Priority:

4. Applicants contend that a certified copy of the 2002-349015 foreign application was submitted to the receiving office under PCT Rule 17 and that the receipt of said documents was acknowledged by the International Bureau. Applicants argue that a copy of the certified priority documents should have been forwarded by WIPO.

It is acknowledged that the certified copies of the foreign priority documents have been received by the USPTO on 27 May 2005, however, a translation of said papers has not been made of record in accordance with 37 CFR § 1.55. See MPEP § 201.15. An English language translation of said documents must be filed together with a statement that the translation of the certified copy is accurate in order for the instant invention to be afforded the benefit of the foreign priority date.

Claim objections

5. Claim 3 is objected to because of the following informalities:

5a. Claim 3, line 2, the term "froth" should be amended to recite "forth".

Appropriate correction is required.

New Rejections:

Claim Rejections - 35 USC § 112, first paragraph:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 3 and 33-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Claims 33-36 are drawn to an isolated protein comprising amino acids 394-532 of SEQ ID NO: 2, wherein proline at position 434 is replaced with a histidine, wherein said protein specifically binds to mammalian Toll- like receptor 3, (TLR3) but fails to induce IFN-β production, a gene encoding such, a recombinant expression vector comprising said gene, a transformed host cell comprising said vector. Thus, the claims encompass a protein that binds to "all possible" mammalian TLR3s. However, the specification teaches that the mutant P434H, wherein the proline at position 434 is replaced with a histidine in the full-length human TICAM-1, (SEQ ID NO:2) had the ability of binding to human TLR3 but lost the ability of inducing the interferon production, (see page 27, paragraph 3). Thus, while the specification discloses that the mutant P434H binds only

to human TLR3 and it does not describe the structure of any other mammalian TLR3 that this mutant might bind to.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus of mammalian TLR3, which the instant protein binds to. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the disclosure of the human TLR3s which the mutant P434H binds to, does not satisfy "all possible" mammalian TLR3s, which mutant P434H should bind to. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the genus of mammalian TLR3s, which the instantly claimed protein might bind to.

Claim Rejections - 35 USC § 112, second paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 3, 33-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7a. Claim 3 recites in lines 4-6 ".....the method comprising causing a candidate compound to be in contact with a cell comprising a vector containing a gene encoding the protein, wherein the toll-like receptor 3 is expressed...", which renders the claim

vague, because it is unclear whether the cell to be used is transfected with a vector comprising a gene encoding the protein of SEQ ID NO:2 or comprises amino acids 394-532 or whether the cell naturally expresses the protein of SEQ ID NO:2, the protein comprising amino acids 394-532 as well as TLR3. The following claim language is suggested for claim 3:

A method of screening for a compound that inhibits the binding between TLR3 and a protein comprising the amino acid of SEQ ID NO:2 or amino acids 394-532 of SEQ ID NO:2, said method comprising contacting a candidate compound with a cell transfected with a gene encoding said protein, wherein said cell naturally expresses TLR3 and measuring whether said compound inhibits the binding between said protein and TLR3.

7b. Claim 3 is indefinite because it is not clear what steps or methods are encompassed by the terms/phrases "...causing a candidate compound..." (in line 5) and "...checking..." (line 8). (Please note that this issue could be overcome by amending these terms/ phrases to recite, for example, "contacting a candidate compound..." and "measuring".)

7c. Claim 33, recites in lines 4-5, ".....having a property of specifically binding to mammalian toll-like receptor 3 but abnormality in a property of inducing interferon β production", which renders the claim confusing, because the phrase is grammatically incorrect and it appears that the two properties are independent of each other, however, the specification shows that the P434H mutant binds to human TLR3, but fails to induce interferon β production. It is suggested that claim 33 be amended as follows:

An isolated protein comprised of amino acid sequence from position 394 to position 532 ~~in~~ of SEQ ID NO: 2, wherein proline at position 434 is replaced with histidine, ~~and having a property of specifically binding to mammalian Toll-like receptor 3 but abnormality in a property of inducing interferon β production~~ wherein said protein specifically binds to human toll-like receptor 3, but fails to induce interferon β production.

Claims 34-36 are rejected under 112, 2nd paragraph so long as they depend on claim 33 for the limitations set forth above.

Claim rejections-35 USC § 103:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Matsuda et al, (WO2002053737-A1, issued on 11 July 2002), in view of Imler, et al (Nature Immunology, Feb 2003, Vol. 4, No. 2, pp. 105-106).

The instant claim 33 is interpreted abs being drawn to a method of screening for a compound that inhibits the binding between TLR3 and a protein that comprises the amino acid of SEQ ID NO:2 or amino acids 394-532 of SEQ ID NO:2, said method comprising contacting a candidate compound with a cell transfected with a gene encoding said protein, wherein said cell expresses TLR3 and measuring whether said compound affects the binding between said protein and TLR3.

Matsuda et al disclose an isolated polypeptide that shares 100% amino acid identity to the polypeptide of SEQ ID NO:2, (TICAM-1) of the instant invention, nucleic acid encoding such, an expression vector comprising said gene and a host cell comprising said vector, (see SEQ ID NO:154,). Also see below, SEQUENCE COMPARISON "C" attached to the office action mailed on 28 December 2007.

However, Matsuda et al reference does not teach that the protein of SEQ ID NO:2 binds TLR3.

Imler et al teach that TICAM-1(SEQ ID NO:2) associates with TLR3 and that it is an essential component of TLR3 signaling, (see page 106, column 1).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the instant invention was made to devise the claimed method of screening for compounds that inhibit the binding between the polypeptide of SEQ ID NO:2 and TLR3,

because Matsuda et al disclose the polypeptide of SEQ ID NO:2 and Imler et al establish that the polypeptide of SEQ ID NO:2 binds TLR3.

One of ordinary skill in the art would have been motivated to combine the teachings of the Matsuda et al and Imler et al and screen for compounds that inhibit the binding between TICAM-1 and TLR3, because TLR3 plays an essential role in the innate immune response against microbial pathogens.

Conclusion:

9. No claim is allowed.

Claim 33-36 are free of prior art of record. An isolated protein comprising amino acids 394-532, wherein proline at position 434 is replaced with a histidine, wherein said protein binds TLR3 but fails to induce interferon beta production, gene encoding said protein, a recombinant expression vector comprising said gene and a transformant cell comprising said vector are novel and unobvious.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FOZIA M. HAMUD whose telephone number is (571)272-0884. The examiner can normally be reached on Monday-Friday: 8:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Art Unit 1647
13 June 2008

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